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RESEARCH

RELATIONSHIP BETWEEN FIBRINOGEN -TO- ALBUMIN RATIO AND ANGIOGRAPHIC NO-REFLOW IN ELDERLY PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION TREATED WITH PRIMARY PERCUTANEOUS CORONARY İNTERVENTION

Abstract

Introduction: Primary percutaneous coronary intervention carries a low success rate and high procedural risk in elderly patients. No-reflow is a serious complication of primary percutaneous coronary intervention in the treatment of acute ST- elevation myocardial infarction. We evaluated whether admission fibrinogen-to-albumin ratio, which has emerged as an inflammatory and haemorheological marker for predicting adverse outcomes in some cardiovascular diseases, predicts angiographic no-reflow in elderly patients with ST-elevation myocardial infarction.

Materials and Method: In total, 617 patients (78.1% men; median age, 75 (68-80years) who underwent primary percutaneous coronary intervention and were admitted within 12 hours from the onset of symptoms were classified into two groups based on the final thrombolysis in myocardial infarction flow grading. No-reflow was defined as post-percutaneous coronary intervention thrombolysis in myocardial infarction grade 0, 1 and 2, and angiographic success (normal reflow) was defined as thrombolysis in myocardial infarction grade 3.

Results: Of the total, 29 (51.8%) patients were found to be frail, 22 (39.3%) were found to be prefrail, and 5 (8.9%) were found be nonfrail. Further, 34 (60.8%) patients were at the risk of malnutrition. Additionally, 38 (67.8%) patients had delirium and 8 (14%) patients died during the postoperative month 1. Although Nutritional Risk Screening 2002 scores positively correlated with first-month mortality, no correlation was found between malnutrition and delirium status. A positive correlation was found between clinical frailty scale score and delirium; however, there was no correlation between clinical frailty scale score and first-month mortality. Positive predictive values of malnutrition and frailty together for first-month mortality increased up to 54.5% from 17.6% and 13.6 and that of delirium increased to 80.2% from 54.5% and 72.4%, respectively.

Conclusion: The incidence of angiographic no-reflow was 19.9% (n = 123). Patients with no-reflow had higher rates of diabetes and smoking, higher thrombus burden and Killip class≥2 on admission and lower baseline left ventricular ejection fraction; they also had increased white blood cell counts, C-reactive protein and fibrinogen-to-albumin ratio levels at admission than the normal flow group. In multivariate analysis, white blood cell count, smoking and fibrinogen-to-albumin ratio were independent predictors of angiographic no-reflow.

Keywords: Aged; Fibrinogen; No-reflow phenomenon; Percutaneous coronary intervention; Serum albumin; St elevation myocardial infarction

ARAŞTIRMA

İLERİ YAŞTA ST YÜKSELMELİ MİYOKARD ENFARKTÜSÜ İLE BAŞVURAN VE PRİMER PERKÜTAN KORONER GİRİŞİM YAPILAN HASTALARDA ANJİYOGRAFİK NO-REFLOW İLE FİBRİNOJEN / ALBÜMİN ORANI ARASINDAKİ İLİŞKİ

Öz

Giriş: Genç hastalarla karşılaştırıldığında, ileri yaş hastalarda primer perkütan koroner girişim, daha düşük başarı ve artmış prosedürel komplikasyonlarla ilişkilidir. No-reflow fenomeni, ST- yükselmeli miyokard enfarktüsü ile primer perkütan koroner girişim yapılan hastalarda karşılaşılabilecek en ciddi komplikasyonlardan biridir. Fibrinojen / albümin oranı; bazı kardiyovasküler hastalıklarda istenmeyen sonlanımları öngördüren, inflamasyon ve hemoreolojiyi yansıtan bir parametre olarak ortaya çıkmıştır. Biz bu çalışmada ST-yükselmeli miyokard enfarktüsü ile başvuran yaşlı hastalarda, başvuru sırasındaki fibrinojen / albümin oranının anjiyografik no-reflow üzerindeki öngördürücülüğünü değerlendirmeyi amaçladık.

Gereç ve Yöntem: Semptom başlangıcından sonra 12 saat içerisinde başvurup primer perkütan koroner girişim yapılan toplam 617 hasta (%78.1 erkek, ortanca yaş: 75 (68-80) yıl) çalışmaya dahil edildi. Hastalar nihai Miyokard Enfarktüsünde Tromboliz akımlarına göre iki gruba ayrıldı. No-reflow işlem sonrası Miyokard Enfarktüsünde Tromboliz 0, 1 ve 2 akım saptanması, anjiyografik başarı ise Miyokard Enfarktüsünde Tromboliz 3 akım saptanması olarak belirlendi.

Bulgular: Anjiyografik no-reflow'un insidansı %19.9 (n =123) olarak saptandı. No-reflow gelişen hastalarda, normal akım grubuna kıyasla hipertansiyon, sigara içiciliği daha sık, trombüs yükü daha fazla ve başvuruda Killip sınıflaması ≥ 2 olma oranı daha yüksek, bazal ejeksiyon fraksiyonu daha düşük, beyaz kan hücre sayısı, yüksek duyarlıklı C-reaktif protein ve fibrinojen/albümin oranı daha yüksek saptandı. Çok değişkenli analizde; beyaz kan hücre sayısı, sigara ve fibrinojen/albümin oranı no-reflow'un bağımsız belirteçleri olarak bulundu.

Sonuç: Sonuç olarak, ST - yükselmeli miyokard enfarktüsü ile başvuran ve perkütan koroner girişim yapılan ileri yaş hastalarda, başvurudaki fibrinojen/albümin oranı anjiyografik no-reflow'un güçlü ve bağımsız bir belirtecidir.

Anahtar sözcükler: Fibrinojen, No-reflow fenomeni; Perkütan koroner girişim; Serum albümini; St yükselmeli miyokard enfarktüsü; Yaşlı

INTRODUCTION

Cardiovascular disorders are the leading cause of morbidity and mortality in persons aged ≥ 65 years; the incidence of these diseases increases with age (1). The elderly population constitutes a growing proportion of patients with acute coronary syndrome (ACS), which includes ST-elevation myocardial infarction (STEMI) (2). Currently, primary percutaneous coronary intervention (PCI) is the preferred way of reperfusion for STEMI, also in elderly patients (3). However, primary PCI carries a low success rate and high procedural risk in older patients than in younger ones. Elderly patients not only possess baseline high-risk features for adverse cardiac events but also have poor procedural characteristics, including poor interventional success and decreased myocardial blush grade, ST-segment resolution and low post-PCI thrombolysis in myocardial infarction (TIMI) grade 3 blood flow (flow grades based on results of the TIMI trial), also called the no-reflow phenomenon (4).

No-reflow is a serious complication of acute STEMI undergoing PCI and is related to larger infarct size and short- and long-term morbidity and mortality (5). The no-reflow phenomenon represents an acute diminution in coronary blood flow despite the presence of normal epicardial coronary artery patency (6). The specific pathophysiological mechanism for its occurrence is still not clearly elucidated, and it is believed that platelet activation and inflammation play a major role in evolving no-reflow (7). Recently, fibrinogen-to-albumin ratio (FAR) has emerged as a feasible and valuable serological marker that may reflect haemorheological and inflammatory status. Elevated FAR concentration has been demonstrated in some cardiovascular diseases and is significantly associated with the severity of coronary stenosis in patients with STEMI (8). To the best of our knowledge, only a limited number of investigations have evaluated the relationship between inflammatory and haemorheological markers such as the CRP, albümin, fibrinogen, FAR and angiographic no-reflow. Moreover, most studies looking at the role of inflammation in no-reflow have been carried out in all-age groups (9, 10), and elderly patients were under-represented in these studies. Therefore this study aimed to investigate the association of inflammatory and hemorheological markers such as fibrinogen, albumin, CRP, FAR with angiographic no-reflow in elderly patients with STEMI in an attempt to explore the predictive value of these indices especially FAR as a novel predictor for elderly AMI patients.

MATERIALS AND METHOD

Study population

The present investigation was a single-center, observational, retrospective cohort study among consecutive elderly patients who were admitted to our tertiary centre with acute STEMI within 12 h of symptom onset and underwent primary PCI between January 2015 and March 2017. All patients were at least 65 years of age. STEMI was defined based on the criteria determined by the European Society of Cardiology and the American College of Cardiology guidelines and was described as classic symptoms of coronary ischaemia for more than 30 min and detection of ST-segment elevation of ≥2.0 mm in men and ≥1.5 mm in women in leads V2–V3 and/or ≥1.0 mm ST-segment elevation in other two contiguous electrocardiography leads or on the presence of a new (or possibly new) left bundle branch block. Patients fulfilling the following criteria were excluded from the study: severe valvular disease, previous history of coronary artery bypass graft, treatment with fibrinolytic agents, cardiogenic shock, renal or hepatic insufficiency, active infection, haematological proliferative diseases, oncological or inflammatory disorders and having no recorded measurement of admission laboratory parameters. The study complied with the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee of our hospital.

Definitions and study endpoints

Hypertension was defined as systolic blood

pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg and/or use of antihypertensive medications. Diabetes was defined as overnight fasting blood glucose ≥126 mg/dL or use of insulin or oral hypoglycaemic agents. Dyslipidaemia was defined as total cholesterol >200 mg/dL, low-density lipoprotein cholesterol >130 mg/dL, Triglycerides >150 mg/dl or use of lipid-lowering drugs. Family history of coronary artery disease (CAD) was defined as having a first-degree male relative who developed CAD before the age of 55 or a first-degree female relative who developed CAD before the age of 65. Patients were classified as smokers if they were actively smoking or had quit smoking within the previous year. The primary endpoint was accepted as the occurrence of no-reflow. Accordingly, the study population were subdivided into normal flow group and no-reflow group.

Laboratory parameters

Peripheral venous blood samples from all patients at the emergency department were collected in tubes with EDTA for haematological tests and dry tubes for biochemical tests and were analysed on priority. Complete blood count measurements were determined using an automated hematology analyzer XE-1200 (Sysmex, Kobe, Japan). Biochemical measurements were performed using a molecular analyzer (Roche Diagnostics, Manheim, Germany). Plasma fibrinogen concentrations were measured using an automatic coagulation analyzer (STA Compact Max, Stago, France). Baseline FAR was calculated using the statistical program (SPSS) by dividing the fibrinogen value with the albumin value.

Echocardiography

Baseline two-dimensional and Doppler echocardiographic examination was performed by experienced echocardiographers for all patients in the intensive coronary care unit to evaluate left ventricular ejection fraction (LVEF) within the first 24–48 h using the same commercially available ultrasound equipment.

Coronary angiography and primary PCI procedure

All primary PCI procedures were performed in our high-volume tertiary cardiology centre with 24 h/7 days PCI facility by expert operators according to the current practice guidelines. Unfractionated heparin 100 U/kg and aspirin 300 mg plus clopidogrel (loading dose 600 mg) were administered to all patients once diagnosed with STEMI in the emergency department. Average door-to-balloon duration was <30 min. Procedural decisions such as stent type, size and length selection and use of adjunctive pharmacotherapy (including glycoprotein IIb/IIIa receptor antagonists) were made by the procedure operators. After stenting, all patients received dual antiplatelet treatment with acetylsalicylic acid (100 mg daily) and clopidogrel (75 mg daily) and were advised to continue these medications for at least 12 months. The TIMI flow grades were evaluated by two interventional cardiologists blinded to the clinical data. The angiographic no-reflow phenomenon was accepted in patients with anterograde TIMI flow grade ≤2 once the recanalisation of the vessel was performed in the absence of dissection, thrombus, spasm or distal embolisation in the final angiogram. Although there is no standard therapy for no-reflow, patients who had no-reflow were treated according to general practice. Intracoronary vasodilatators, glicoprotein IIb/IIIa inhibitor and aspiration thrombectomy were administered at the discretion of the operator.

Multivessel disease was described as presence of ≥1 lesion with >50% stenosis in ≥1 major epicardial coronary artery or its major branches distant from the infarct related artery. To assess thrombus burden we used the TIMI thrombus scale (11). TIMI thrombus grade 0, no angiographic characteristics of thrombus are present; TIMI thrombus grade 1, possible thrombus with angiographic characteristics include declined contrast density, haziness, irregular lesion contour, or a smooth convex "meniscus" at the site of total occlusion suggestive but not diagnostic of thrombus; TIMI thrombus grade 2, definite

thrombus is present in multiple angiographic views, with the largest dimensions ≤1/2 the vessel diameter; in TIMI thrombus grade 3, definite thrombus in multiple views but with the greatest linear dimension>1/2 but <2 vessel diameters; TIMI thrombus grade 4, definite large thrombus, with the greatest dimension ≥2 vessel diameters; TIMI thrombus grade 5, there is complete thrombotic occlusion of the vessel. TIMI thrombus grade ≥4 was accepted as high grade angiographic thrombus burden (12). Pre-procedural collateral flow was determined according to Rentrop classification: any visible filling of collaterals was considered grade 0, filling of side branches without epicardial segments was classified as grade 1, partial filling of epicardial segments was classified as grade 2, and complete filling of epicardial segments was considered grade 3(9). Rentrop grade 0 and 1was accepted as poor collateral flow (13).

Statistical analysis

Statistical analysis was performed using SPSS 22.0 Statistical Package Program for Windows (SPSS, Inc., IL, USA). Continuous variables were presented as mean ± SD and median with interquartile ranges as appropriate and categorical variables as frequency and percentage. To test normality of distribution, the Kolmogorov–Smirnov test was used. Differences between groups were evaluated using Student's t-test for normally distributed variables and Mann-Whitney U test test for variables without normal distribution. The Chi square or Fisher's exact test was used to compare categorical variables. We first used univariate analysis to examine the association of each variable with angiographic no-reflow. To assess the effects of parameters that were significant in univariate analysis ($p < 0.05$), we used multivariate logistic regression. The receiver operating characteristic (ROC) curve was used to determine an optimal cut-off value for FAR according to the Youden's index. The correlation between FAR and hsCRP was assessed using Spearman's correlation test. A p value of <0.05 (using a two-sided test) was considered significant.

RESULTS

The baseline clinical, laboratory and angiographic characteristics of patients with and without no-reflow are summarised in Table 1. Of 617 patients, 78.1% were male and the median (interquartile range) age was 75 (68–80) years. Angiographic no-reflow was developed in 123 (19.9%) patients. Study patients were divided into two groups based on their TIMI flow grades after primary PCI. Patients with no-reflow exhibited a higher rate of diabetes mellitus, smoking and lower LVEF compared with those without no-reflow. Also no-reflow group had higher thrombus burden and high rates of Killip class ≥2 on admission when compared to that of reflow group. The no-reflow group had significantly higher white blood cell (WBC) counts and fibrinogen and hsCRP levels and lower albumin levels than those in the reflow group.

Patient FAR values were significantly higher in the no-reflow group than in the normal flow group ($p <.001$; Figure 1). There was no statistically significant difference in angiographic characteristics between the two groups.

The ROC curve analysis explored the discriminatory capability of admission FAR for no-reflow. The area under the curve was 0.810 (95% CI, 0.765–0.856; $p < 0.001$). Using a cut-off level of 75.0, FAR predicted angiographic no-reflow with a sensitivity of 76% and specificity of 76% (Figure 2).

Univariate and multivariate logistic regression analyses of the relationship between the no-reflow phenomenon and multiple parameters are listed in Table 2. On univariate logistic regression analysis, the FAR values demonstrated a strong relation with the no-reflow phenomenon ($p <.001$). The other univariate predictors of no-reflow were smoking, diabetes mellitus, LVEF, high TIMI thrombus grade, high Killip class on admission, WBC, hsCRP, fibrinogen and albumin levels. When constructed, a multivariate logistic regression including all the following significant univariate predictors: WBC (odds ratio [OR], 1.679; 95% confidence interval [CI],

1.446–1.949; p <.001); smoking (OR, 1.918; 95% CI, 1.165–3.159; p =.010) and FAR levels >75.0 (OR, 6.968; 95% CI, 4.091–11.869; p <.001) were identified as independent predictors of angiographic no-reflow.

In the correlation analysis, FAR values had a significantly positive correlation with the hsCRP level (r = 0.385, p < 0.001) (Figure 3).

DISCUSSION

This study demonstrated that FAR was independently associated with angiographic no-reflow phenomenon in elderly patients with STEMI. Patients with elevated FAR levels had higher risks for this complication. FAR was also positively correlated with serum hsCRP levels, demonstrating its strong relationship with systemic inflammation.

Elderly patients are at higher risks than younger patients if they present with STEMI. Elderly patients are often frail and have extensive CAD, which elevates the risk of morbidity and mortality. Other reasons for higher risk include atypical presentation and delays in seeking medical care (2). Trials regarding ACS and revascularisation have selectively excluded elderly patients because of potentially high mortality rates. Thus, most of the evidence has been extrapolated from the studies consisting of younger patients, which impedes extending the findings of these studies to the elderly population that experiences the worst cardiac outcomes (14).

It is well known that in elderly patients, the primary PCI success rate is lower than in younger patients; outcomes after the procedure are worse, with higher risks of PCI complications. Despite similar frequencies of TIMI flow before PCI, older patients are less likely to achieve optimal epicardial flow (TIMI grade 3 flow) and ST-segment resolution after PCI (15). The presence of complex coronary anatomy frequently observed in older patients may be associated with a higher rate of distal embolisation, which is a significant determinant of myocardial perfusion and long-term clinical outcome after primary PCI(16). In addition, several studies have underlined that older patients are more likely to have no reflow phenomenon, probably linked to co-morbidities and more severe coronary artery disease (17, 18). De Luca et al demonstrated a relationship between older age and impaired myocardial perfusion evaluated by myocardial blush grade as well as ST-segment resolution. Furthermore, age and poor myocardial flow- perfusion were shown to be independently related with 1-year mortality (19). Therefore, early identification of elderly patients with high risks of impaired myocardial perfusion and coronary angiographic no-reflow is essential.

The pathophysiological mechanisms of coronary no-reflow are presently not exactly understood. Previous studies demonstrated that no-reflow is related to a diverse set of pathological factors, such as coagulation cascade via endothelial dysfunction, microvascular obstruction caused by distal embolisation, action of reactive oxygen species, ischaemia–reperfusion injury, platelet aggregation, haemorheological alterations and complicated interaction between leukocytes and platelets activated by the inflammatory process (20).

Fibrinogen and albumin are widely utilised and are significant factors in responses to systemic inflammatory and haemorheological changes. Fibrinogen is known to be a precursor of fibrin and stimulates platelet aggregation. Fibrinogen is also an acute phase protein with positive pro-inflammatory effects. Fibrinogen was shown to upregulate the synthesis of pro-inflammatory cytokines, including interleukin-1 and tumour necrosis factor alpha. These cytokines inhibit the arrangement of stable fibrous caps and mediate increased adhesion molecule expression; they also culminate in endothelial dysfunction and thrombus formation (21). Therefore, these alterations could further generate the activation and rupture of atherosclerotic plaque and the resulting thrombosis. Additionally, elevated fibrinogen levels are related with increased plasma viscosity, which further causes diminished blood flow velocity and finally increases

the risk of thrombosis (22). Increased concentration of fibrinogen has been shown to increase the risk of thrombosis and is an independent predictor of coronary heart disease and myocardial infarction (MI) according to the findings of previous studies (23).

Serum albumin is the major protein in human serum, which is the main component that maintains plasma oncotic pressure; it participates in acute and chronic inflammatory reactions (24). Albumin is one of the main factors affecting plasma viscosity, which plays an important role in inhibiting platelet activation and aggregation and might negatively correlate with erythrocyte aggregation (25). Previous studies demonstrated that serum albumin levels are closely associated with the occurrence, development and severity of coronary heart disease (26). Recent studies also reported that decreased concentration of albumin is a risk factor for incident acute MI in patients with CAD and is related to elevated cardiovascular morbidity and long-term outcomes (27). Furthermore, hypoalbuminemia can predict the occurrence of the no-flow phenomenon in patients with STEMI after PCI (28).

Based on the previous study results, both elevated fibrinogen levels and lower serum albumin levels were demonstrated to be associated with adverse cardiac outcomes in STEMI. FAR, which comprises these two predictors, is an important serological marker that may provide information on both haemorheology and inflammation in patients with STEMI. It has been shown that there is a positive correlation between FAR and SYNTAX score in patients with STEMI, and FAR can be utilised as an independent marker of elevated SYNTAX score and the severity of coronary stenosis in STEMI [8]. Xiao et al. (29) found that preoperative FAR was an independent prognostic factor in STEMI patients undergoing primary PCI and might improve risk stratification in patients with STEMI. Recently, Zhao et al. (9) reported that admission FAR levels were associated significantly and independently with angiographic no-reflow and short-term mortality in 510 patients with STEMI undergoing pPCI. In addition, fibrinogen and hs-CRP were significantly higher among patients with no-reflow in all-age groups. According to their results, the mean age of the study population was 61.14 ± 11.15 and compared to normal-reflow group, patients in the no-reflow group were significantly older (64.09 ± 11.53 vs.60.44 ± 10.96 years). In another recent study, Del Turco et al. (30) evaluated 625 patients with STEMI and demonstrated that elderly patients had significantly higher values of BNP, leukocytes, CRP-to-albumin ratio (CAR), fibrinogen and lower serum albumin levels compared with young patients. In elderly patients, higher levels of CAR, fibrinogen and leukocytes were significantly associated with no-reflow similar to our study results. Conversely, in young patients, BNP level on admission was the only laboratory parameter associated with no-reflow. Thus their findings showed a differential inflammatory pattern between young and elderly STEMI patients at the hospital admission that confirms the presence of a higher acute proinflammatory systemic response and chronic low-grade inflammatory status typical of aging in elderly patients. In the light of these findings, one may conclude that benefits of FAR, as a combination of fibrinogen and albumin might be more impressive in the aging patients. Therefore, this retrospective study was undertaken to evaluate whether clinical benefits of FAR as predictor of no-reflow in the aged could be validated in the setting of STEMI. As expected, FAR level on admission was found as a strong predictor of no-reflow in elderly patients with STEMI in our study.

Several reports have shown that multivessel disease is frequently associated with no-reflow phenomenon (31). In the current study, there were no differences with respect to the ratio of multivessel disease between no-reflow and reflow groups. It is known that older patients have a higher number of affected vessels compared to younger patients (32). In our study, an age-dependent high frequency of multivessel disease in both groups may be the underlying mechanism of the non-significant effect

of multivessel disease on the presence of no-reflow against the results of previous several studies evaluating all-age groups.

In agreement with the literature, our results suggest that inflammation and haemorheological alterations play an important role in no-reflow pathophysiology and parameters that can directly or indirectly reflect inflammation and that blood viscosity can play a substantial role in the success rate of primary PCI in elderly patients with STEMI. Our results demonstrated that admission FAR levels were significantly higher in the no-reflow group compared with the normal flow group. FAR values predicted the no-reflow phenomenon with good sensitivity and specificity. Clinically, as a new marker of inflammation and haemorheology, FAR may be used to identify patients at a high risk for evolution of no-reflow phenomenon. At present, there is no consensus on how to best manage no-reflow. As no-reflow is related with adverse cardiovascular events, accurate prediction of no-reflow could ameliorate the outcomes of patients by close monitoring. Accurate risk stratification for the occurrence of no-reflow might help deciding on the most effective measures aimed at preventing this entity and using certain techniques that may ameliorate the degree of noreflow in the setting of acute MI. Such prevention strategies include a shortened door-to-balloon time, more effective antiplatelet drug therapies (prasugrel or tikagrelor), primary stenting, avoidance of high pressure stent deployment, and aspiration thrombectomy before the stent implantation in this high-risk population with STEMI (33).

Limitations

This study has some limitations. First, this was a retrospective single-centre study with cross-sectional design. Although a relatively large series of elderly patients with STEMI were examined, the study population was limited in size. This factor may limit the power of statistical analyses. In addition, we did not evaluate several risk factors for the no-reflow phenomenon, and it might have influenced the multivariate test results. We evaluated FAR values only once during admission; potential temporal changes were not examined in this study. Absence of other inflammatory markers, except for hsCRP, was another limitation of this study. We only showed a relationship between FAR and angiographic no-reflow rather than a causal association. Although the purpose of our study was not to investigate the association between FAR and in-hospital mortality, it would be better if we had followed the patients and investigate the relationship between short term mortality and FAR in these patients. Prospectively designed studies on larger elderly cohorts are required to validate our findings, reveal the underlying mechanism and elucidate the utility of FAR in elderly AMI patients.

CONCLUSIONS

This study is the first to focus on the relationship of admission FAR values with angiographic no-reflow among elderly patients with STEMI. Our findings revealed that higher FAR levels were significantly and independently associated with the no-reflow phenomenon.

Furthermore, preprocedural FAR values may be useful in reflecting the inflammatory status and haemorheological alterations in elderly patients. As a low-cost, simple, reproducible parameter, FAR can be used in routine clinical practise in predicting no-reflow. Nevertheless, our findings should be confirmed by prospective and large-scale studies, including other inflammatory biomarkers, to determine the precise role of FAR in elderly patients with STEMI.

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None

CONFLICTS OF INTEREST

The authors of this article state that they have no conflict of interest.

Table 1. Baseline clinical, laboratory and angographic characteristics of the study population according to the presence of angiographic no-reflow.

Variable	Total n = 617	No-reflow (+) n = 123	No-reflow (–) n = 494	p value
Age	75 (68-80)	76 (68-81)	75 (68-80)	.167
Gender, Male n (%)	482 (78.1 %)	90 (73.2 %)	392 (79.4 %)	.138
Hypertension, n (%)	342 (55.4 %)	62 (50.4 %)	280 (56.7 %)	.210
Diabetes, n (%)	232 (37.6 %)	56 (45.5 %)	176 (35.6 %)	.043
Smoking, n (%)	235 (38.1 %)	59 (48.0 %)	176 (35.6 %)	.012
Hyperlipidemia, n (%)	367 (59.5 %)	82 (66.7%)	285 (57.7 %)	.070
Family History of CAD, n (%)	120 (19.4 %)	24 (19.5 %)	96 (19.4 %)	.984
Body-mass index (kg/m^2)	23.3 ± 2.7	22.9 ± 2.6	23.4 ± 2.7	.093
LVEF (%)	45 (42-50)	43(42-48)	43(40-48)	.027
Heart rate (bpm)	79.9 ± 11.6	81.5 ±10.8	79.5 ± 11.8	.091
Killip class ≥2	162 (26.3 %)	42 (34.1 %)	120 (24.3 %)	.026
Medical therapy				
Aspirin, n (%)	278 (45.1%)	60 (48.8%)	218 (44.1 %)	.354
ß blocker, n (%)	462 (74.9 %)	88 (71.5 %)	374 (75.7%)	.341
Statin, n (%)	299 (48.5 %)	54 (43.9 %)	245 (49.6 %)	.258
ACE inh/ARB n (%)	384 (62.4 %)	72 (59.5%)	312 (63.2%)	.457
Diuretic, n (%)	97 (15.7 %)	23 (18.7 %)	74 (15.0 %)	.311
Angiographic characteristics	2.9 ± 0.3	2.9 ± 0.4	2.9 ± 0.3	.396
Stent length (mm)	20 (18-23)	20 (17-25)	20 (19-23)	.780
Total number of stents	1.8 ± 0.5	1.8 ± 0.5	1.8 ± 0.5	.281
High-grade thrombus burden, n (%)	440 (71.3 %)	99 (80.5 %)	341 (69 %)	.012
Collateral flow ≤1, n (%)	133 (21.6 %)	33 (26.8 %)	100 (20.2 %)	.112
Use of GpIIb/IIIa inhibitor, n (%)	31 (5.0 %)	10 (8.1%)	21 (4.3 %)	.078
Pain to balloon time (min)	301±128	320 ± 133)	296 ± 126	.065

Variable	Total n = 617	No-reflow (+) n = 123	No-reflow (–) n = 494	p value
DES, n (%)	138 (22.4 %)	24 (19.5 %)	114 (23.1%)	.396
Number of affected vessels	1.8 ± 0.5	1.8 ± 0.5	1.9 ± 0.5	.054
Multivessel disease, n (%)	464 (75.2 %)	98 (79.7 %)	366 (74.1 %)	.199
Laboratory parameters				
Hemoglobin (g/dl)	13.9 (12.5-14.9)	14.5 (13.0-15.6)	14.4 (13.0-15.3)	.561
WBC (×103 µL)	8.0 ±1.8	9.3 ±1.5	7.7 ±1.8	<.001
Platelet (×103 µL)	254 ± 69	262 ± 61	253 ± 71	.188
Glucose, mg/dL	101 (91-130)	102 (90-131)	101 (92-130)	.732
Creatinine (mg/dl)	0.9 (0.8-1.0)	0.9 (0.8-1.0)	0.9 (0.8-1.0)	.072
Urea (mg/dl)	35 (28-43)	33 (28-42)	36 (28-44)	.195
Total cholesterol (mg/dL)	175 ± 41	174 ± 41	175 ± 42	.806
Triglycerides (mg/dL)	141 (100-190)	150 (112-194)	138 (100-186)	.098
LDL cholesterol (mg/dL)	105 (82-130)	101 (80-132)	105 (82-127)	.819
HDL-C (mg/dl)	40 (33-47)	39 (33-45)	40 (33-48)	.444
Albumin (g/dl)	3.9 ± 0.5	3.8 ± 0.7	4.0 ± 0.4	.005
hsCRP (mg/dl)	2.5 (1.2-5.0)	5.0 (2.0-7.0)	2.4 (1.1-4.8)	<.001
Fibrinogen	305 ± 62	318 ± 78	302 ± 56	.011
Fibrinogen to albumin ratio	71 ± 13	83 ± 10	68 ± 11	<.001

Data are presented mean ± SD or n (%).

ACE: Angiotensin converting enzyme; ARB: Angiotensin II receptor blocker; CAD: coronary artery disease; DES: Drug-eluting stent; HDL-C: high-density lipoprotein cholesterol; FAR: fibrinogen to albümin ratio; HDL-C: high-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; WBC: white blood cell;

Table 2. Univariate and multivariate logistic regression analysis for prediction of angiographic no-reflow.

Variable	OR	Univariate analysis 95 % CI	P Value	OR	Univariate analysis 95 % CI	P Value
Age	1.027	0.997-1.058	0.076			
Gender, male	0.710	0.450-1.118	0.139			
Hypertension	0.777	0.523-1.154	0.211			
Diabetes	1.510	1.013-2.252	0.043	1.333	0.820-2.165	0.246
Smoking	1.666	1.118-2.482	0.012	1.918	1.165-3.159	0.010
Hyperlipidemia	1.467	0.968-2.222	0.071			
Family history of CAD	1.005	0.610-1.655	0.984			
Body-mass index	0.940	0.874-1.010	0.093			
LVEF (%)	0.957	0.921-0.994	0.024	0.979	0.935-1.024	0.348
Heart rate	1.015	0.998-1.032	0.091			
Killip class ≥2	1.798	1.181-2.738	0.006	1.261	0.738-2.156	0.396
Aspirin	1.206	0.812-1.791	0.354			
β-blocker	0.807	0.518-1.256	0.341			
Statin	0.795	0.535-1.183	0.259			
ACE inh /ARB	0.857	0.571-1.287	0.457			
Diuretic	1.305	0.779-2.187	0.312			
Stent diameter	0.788	0.455-1.365	0.396			
Stent lenght	0.993	0.949-1.039	0.757			
Total number of stents	0.814	0.560-1.183	0.280			
Use of Gp2b/3a inhibitor	1.993	0.913-4.350	0.083			
Pain to balloon time	1.001	1.000-1.003	0.066			
DES	0.808	0.494-1.322	0.397			
High-grade thrombus burden	2.179	1.313-3.618	0.003	1.049	0.539-2.042	0.888
Collateral flow ≤1	1.445	0.916-2.278	0.113			
Multivessel disease	1.371	0.846-2.222	0.201			
Number of affected vessels	0.696	0.481-1.007	0.055			

Variable	OR	Univariate analysis 95 % CI	P Value	OR	Univariate analysis 95 % CI	P Value
Hemoglobin (g/dl)	1.071	0.982-1.167	0.122			
Platelet (×103 µL)	1.002	0.999-1.005	0.188			
WBC (×103 µL)	1.756	1.534-2.011	<.001	1.679	1.446-1.949	<.001
Glucose (mg/dl)	0.996	0.995-1.004	0.325			
Creatinine (mg/dl)	1.670	0.798-3.495	0.174			
Urea (mg(dl)	0.999	0.986-1.013	0.937			
Total cholesterol (mg/dl)	0.999	0.995-1.004	0.806			
Triglycerides (mg/dl)	1.002	0.999-1.004	0.147			
LDL cholesterol (mg/dL)	0.999	0.994-1.005	0.838			
HDL-C (mg/dl)	0.996	0.978-1.014	0.644			
Albumin (g/dl)	0.499	0.344-0.725	<.001			
hsCRP (mg/dl)	1.150	1.079-1.226	0.001	0.952-1.134	0.197	
Fibrinogen	1.004	1.001-1.007	0.012			
Fibrinogen to albumin ratio	1.117	1.093-1.142	<.001			
FAR >75.0	10.328	6.489-16.441	<.001	4.091-11.869	<.001	

ACE: Angiotensin converting enzyme; ARB: Angiotensin II receptor blocker; CAD: coronary artery disease; DES: Drug-eluting stent; HDL-C: high-density lipoprotein cholesterol; FAR: fibrinogen to albümin ratio; HDL-C: high-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; WBC: white blood cell;

Figure 1. Box plot presentation comparison of fibrinogen to albumin ratio.

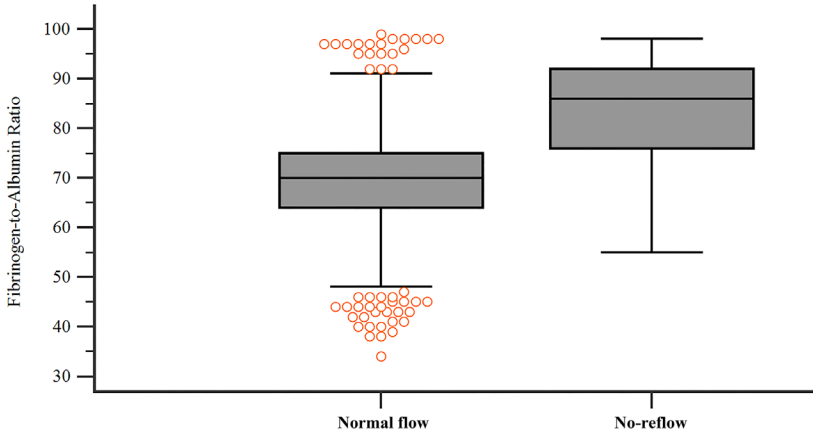


Figure 2. ROC curve analysis of fibrinogen to albumin ratio to predict no-reflow

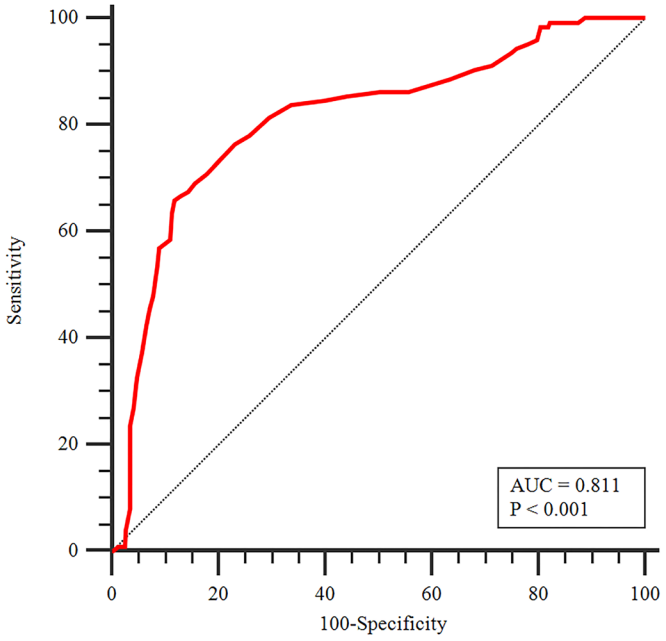
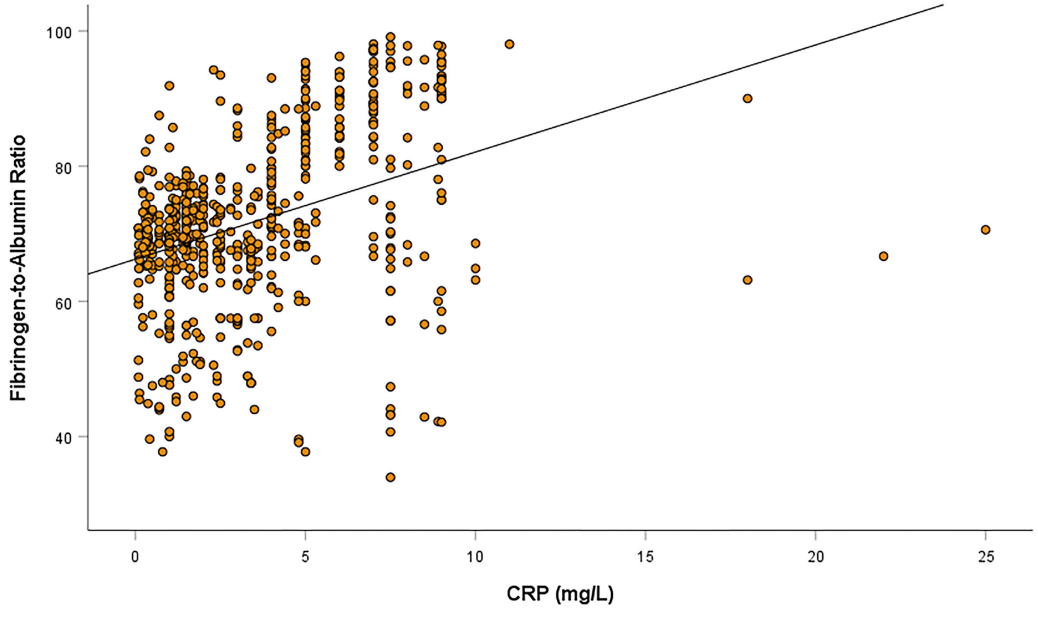


Figure 3. Correlation analysis of fibrinogen to albumin ratio with CRP level.



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